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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,605	02/26/2002	Keith M Skubitz	09531-203US1	3442

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EXAMINER	
EMCH, GREGORY S	
ART UNIT	PAPER NUMBER
1649	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/069,605	SKUBITZ ET AL.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-10,19-22 and 27-31* is/are pending in the application.

4a) Of the above claim(s) *19-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 2,5-10 and 27-31* is/are rejected.

7)☒ Claim(s) *2* is/are objected to.

8)☒ Claim(s) *1,2,5-10,19-22 and 27-31* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission filed on 22 January 2008 has been entered.

Response to Amendment

Claims 1 and 27 have been amended as requested in the amendment filed on 22 January 2008. Following the amendment, claims 1, 2, 5-10, 19-22 and 27-31 are pending in the instant application.

Claims 19-22 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1, 2, 5-10 and 27-31 are under examination in the instant office action.

Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicants' response and withdrawn.

Claim Objections

Claims 1, 2 and 27 are objected to because of the following informalities: The claims recite the phrase "represented by SEQ ID NO: 14." This is not a conventional transitional term as outlined in MPEP § 2111.03. Thus, the scope of the claims is not clearly defined. Appropriate correction is required.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1, 2, 5-10 and 27-31 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for reasons of record and as set forth below. The claim contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

In the reply filed on 22 January 2008, Applicants assert that they have amended claims 1 and 27 to replace "biologically active analogs" with "biologically active fragments." Applicants assert that U.S. Application No. 10/469,273 (published as US 2004/0214184), which names the same inventors as the present application, discloses the effectiveness of over 75 different fragments of the peptide having the sequence of SEQ ID NO: 14 (referred to as SEQ ID NO: 1, S28 and CD66a-24 in U.S. Application No. 10/469,273). Applicants assert that Paragraph [0064] in U.S. Application No.

10/469,273 states that "[e]ach of the smaller peptides (S 180, S181, and S182) had activity in the T-cell activation assay (FIG. 3), demonstrating that the entire amino acid sequence of S28 is not required for activity." Thus, Applicants assert that the claims meet the enablement and written description requirements of 35 U.S.C. 112, first paragraph.

Applicants' arguments have been fully considered and are not found persuasive.

Applicants argue that the specification contains an adequate written description of the claimed subject matter because the claims contain a function (decreases homotypic adhesion among CD66a family members) and a structural limitation (fragment of SEQ ID NO: 14). However, in the University of California v. Eli Lilly and Co., 43 USPQ2d 1398 (Fed. Cir. 1997), the court held that one of two elements may satisfy a genus of cDNAs: i) a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or; ii) a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus.). In the instant case, the first element is not met because only a cDNA encoding SEQ ID NO: 14 is disclosed. The second element requires structural features common to members of the genus. However, in the instant disclosure, insufficient guidance is provided as to which are the critical residues that are necessary for the claimed peptide function of decreasing homotypic adhesion among CD66a family members. Applicants assert that the disclosure of US 2004/0214184 provides the requisite written description both structurally and functionally for the claimed fragments of SEQ ID NO: 14, e.g., in paragraph [0064] of the '184 document. However, examining the disclosure of the ‘184

document reveals that S28 (the instant peptide of SEQ ID NO: 14) has modest activity in a T-cell activation assay when compared to control (see Figure 1). Figure 3 of the '184 document reveals that one fragment (referred to as S181) of the peptide of SEQ ID NO: 14 had similar activity to the full peptide in the same assay. The other two fragments analyzed (i.e. S180 and S182) had no such activity as the amount of T-cell activation induced by these fragments was less than the negative control. Accordingly, a provision of 1 species is insufficient to fulfill the written description requirement of 35 U.S.C. 112, first paragraph. Regardless, inducing T-cell activation is not the same as the claimed function of decreasing homotypic adhesion among CD66 family members.

Therefore, as set forth previously, with the exception of the complete peptide of SEQ ID NO: 14, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Therefore, only isolated peptides comprising the complete, unaltered amino acid sequences set forth in SEQ ID NO: 14, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. Applicants are reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The scope of enablement rejection of claims 1, 2, 5-10 and 27-31 under 35 U.S.C. 112, first paragraph, is maintained for reasons of record and as set forth below. This is because the specification, while being enabling for the peptide of SEQ ID NO: 14 and methods thereof, does not reasonably provide enablement for peptides and biologically active fragments of SEQ ID NO: 14 and methods thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

Applicants assertions of the current claims meeting the enablement requirement are set forth above and are not persuasive as set forth above and below.

The instant claims require the use of a broad genus of peptides and as stated above, Applicants have not described all of the common features of the genus such that the skilled artisan could identify individual members. The potential amino acid sequences encompassed by the claim have particular structures, the predictability of which is complex and outside the realm of routine experimentation. Since detailed information regarding the structural requirements of the multitude of potential amino acid sequences encompassed by the claims are lacking, and given the lack of working

examples reciting any and all of the sequences encompassed by the claims, it is unpredictable as to which variations, if any, meet the limitations of the claims. Thus, making said peptides or polypeptides and testing them for the claimed biological activity would constitute undue experimentation.

Relevant art regarding biliary glycoprotein (BGP; i.e., an amino acid molecule comprising SEQ ID NO: 14) and BGP splice variants, including those with fragments of SEQ ID NO: 14, often have divergent functions. Specifically, Barnett et al (cited previously) teaches that BGP isoforms probably have diverse *in vivo* functions and that fusions comprising the extracellular domain of BGPa and an Fc immunoglobulin fragment and a BGPb-Fc have different functions (p.1280, ¶ 2 and 3). Thus, the predictability of amino acid sequences that would function as claimed is complex and outside the realm of routine experimentation.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. Due to the large quantity of experimentation necessary to practice the claimed invention, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the claimed methods, and the breadth of the claims which encompass variant proteins, undue experimentation would be required of the skilled artisan to practice the claimed invention in its full scope.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Upon further consideration, the rejection of claims 1, 5-10 and 27-31 under 35 U.S.C. 102(b) as being anticipated by Watt et al. (item AFFFF on IDS dated 10 December 2004) is hereby reinstated. It is noted that for the purposes of this rejection, the term "represented by" in claim 2 is being interpreted as closed language (or as "consisting of").

The claims are drawn to an isolated peptide comprising an amino acid sequence represented by SEQ ID NO: 14, or analog thereof that modulates the function of at least one CD66 family member and/or at least one ligand thereof; and a method of modulating immune cell activation, proliferation, and/or differentiation, comprising contacting an immune cell with at least one peptide or peptide conjugate comprising an amino acid sequence represented by SEQ ID NO: 14.

The Watt et al. reference teaches biliary glycoprotein (BGP) and splice variants (e.g., BGPc) that comprise an amino acid sequence that is 100% identical with the instant SEQ ID NO: 14, which binds specifically to CD66 monoclonal antibodies (abstract). The Watt et al. reference also teaches that BGP and BGPc localize at the cell surface at areas of cell-cell contact and that they mediate homotypic adhesion (p.205, ¶1 and 2). Although the Watt et al. reference does not appreciate the recited

property of the claimed peptide, i.e. decreasing homotypic adhesion among CD66a family members, this is nonetheless an inherent property of the polypeptide described therein. Applicants are reminded that chemical compounds and their properties are inseparable (In re Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA1963)), as are their processes and yields (In re Von Schickh, 362 F.2d 821, 150 USPQ 300 (CCPA 1966)). Therefore, absent evidence to the contrary, the Watt et al. reference inherently teaches the claimed function since it teaches an amino acid molecule that comprises the instant SEQ ID NO: 14, thus meeting the limitations of claim 1.

Additionally, the Watt et al. reference teaches BGPc-cellular fusions, (e.g., CHO-BGPc; p.205, ¶1), thus meeting the limitations of claims 5-7. Further, the reference teaches the peptide attached to a fluorescent tag (p.202, ¶1), thus meeting the limitations of claims 8-10. The reference teaches contacting immune cells and epithelial cells (i.e. T-cells, B-cells, myeloid, erythroid and colonic epithelial cells) with BGPc and teaches that BGPc mediates homotypic adhesion, which can encompass decreasing homotypic adhesion. As referred to above, although the Watt et al. reference does not explicitly appreciate decreasing homotypic adhesion, this is nonetheless an inherent property of the polypeptide(s) described therein, since the reference meets the structural limitations of the claims. Therefore, the limitations of claims 27-30 have been met. It is noted that the claimed "method of modulating immune cell activation, proliferation, and/or differentiation" (as recited by claim 27) is the purpose of the invention, which is recited by the preamble and thus imparts no patentable weight on the claim (see MPEP 2111.02, section II). Regardless, the reference teaches

modulating immune cell activation, since it teaches adhesion of BGPc expressing cells with macrophage cells (p.205, figure 6), for example. Finally, the reference teaches *in vivo* studies (p.208, final paragraph), thus meeting the limitations of claim 31.

In the reply filed on 07 September 2007, Applicants assert, "Watt et al. does not specifically call out the fragment of BGP that Applicants' claims recite (i.e., SEQ ID NO: 14). Watt et al. further does not disclose that BGP or any portion thereof could decrease homotypic adhesion among CD66a family members."

Applicants' arguments have been fully considered and are not found persuasive. There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure *at the time of invention*, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003) (see MPEP § 2112, section II). Again, since the reference teaches an amino acid molecule that comprises the claimed SEQ ID NO: 14, the reference inherently teaches the claimed function. It is irrelevant that the reference did not explicitly appreciate this inherent function. It is noted that the disclosure of the Watt et al. reference does not lack any element provided by the claims of the instant application, i.e., the instant claims require no more than is taught by the Watt et al. reference. Since the Watt et al. reference teaches all the elements of the claims (both expressly and inherently), the patent anticipates the claimed invention.

Upon further consideration, the rejection of claims 1, 5-7 and 27, 28 and 30 under 35 U.S.C. 102(b) as being anticipated by Barnett et al (Mol. Cell. Biol. 13: 1273-

1282, 1993, cited previously) is hereby reinstated. It is again noted that for the purposes of this rejection, the term "represented by" in claim 2 is being interpreted as closed language (or as "consisting of").

The claims are drawn to an isolated peptide comprising an amino acid sequence represented by SEQ ID NO: 14, or analog thereof that modulates the function of at least one CD66 family member and/or at least one ligand thereof; and a method of modulating immune cell activation, proliferation, and/or differentiation, comprising contacting an immune cell with at least one peptide or peptide conjugate comprising an amino acid sequence represented by SEQ ID NO: 14.

The Barnett et al. reference teaches biliary glycoprotein (BGP) that comprises an extracellular domain (II a), which comprises an amino acid sequence which is 100% identical with the instant SEQ ID NO: 14 (see Figure 5B, p.1279). The Barnett et al document also teaches that the BGPs are members of the CD66 family (p1273, ¶1). Although the Barnett et al. reference does not appreciate the recited property of the claimed peptide, i.e. decreasing homotypic adhesion among CD66a family members, this is nonetheless an inherent property of the polypeptide described therein. Applicants are reminded that chemical compounds and their properties are inseparable (In re Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA1963)), as are their processes and yields (In re Von Schickh, 362 F.2d 821, 150 USPQ 300 (CCPA 1966)). Therefore, absent evidence to the contrary, the Barnett et al. reference inherently teaches the claimed function since it teaches an amino acid molecule that comprises the instant SEQ ID NO: 14, thus meeting the limitations of claim 1.

Furthermore, the Barnett et al. reference teaches contacting immune cells and epithelial cells (e.g. acute myelogenous leukemia cells and human colonic mucosal cells) with various BGP isoantigens (p.1274, ¶1 and p.1278, ¶3) and teaches that BGPs (BGPa and BGPb) mediate homotypic adhesion (p.1280, ¶1), which can encompass decreasing homotypic adhesion. As referred to above, although the Barnett et al. reference does not explicitly appreciate decreasing homotypic adhesion, this is nonetheless an inherent property of the polypeptide(s) described therein, since the reference meets the structural limitations of the claims. Therefore, the limitations of claims 27, 28 and 30 have been met. It is also again noted that the claimed "method of modulating immune cell activation, proliferation, and/or differentiation" (as recited by claim 27) is the purpose of the invention, which is recited by the preamble and thus imparts no patentable weight on the claim (see MPEP 2111.02, section II).

Additionally, the Barnett et al. reference teaches fusion proteins, comprising the extracellular domain of either BGPa or BGPb conjugated to a human Fc fragment (p.1280, ¶3), and teaches expression of the BGP isoantigens in various cells, i.e., the peptide complexed with cells (p.1274, ¶1), thus meeting the limitations of claims 5-7.

In the reply filed on 07 September 2007, Applicants assert, "Barnett et al. does not specifically call out the sequence of any BGP, and also does not disclose the particular sequence that Applicants' claims recite (i.e., SEQ ID NO: 14). Although Barnett et al. suggests that BGPs may function as class-specific homotypic adhesion proteins, Barnett et al. does not disclose that the claimed portion of BGP (i.e., SEQ ID

NO: 14) could decrease homotypic adhesion among CD66a family members while other portions may, for example, decrease heterotypic adhesion, increase homotypic or heterotypic adhesion, or modify homotypic or heterotypic adhesion between CD66 family members from a group other than CD66a."

Applicants' arguments have been fully considered and are not found persuasive. There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure *at the time of invention*, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003) (see MPEP § 2112, section II). Since the reference teaches an amino acid molecule that comprises the claimed SEQ ID NO: 14, the reference inherently teaches its claimed function. Since the reference teaches an amino acid molecule that comprises the claimed SEQ ID NO: 14, the reference inherently teaches the claimed function. It is irrelevant that the reference did not explicitly appreciate this inherent function. It is noted that the disclosure of the Barnett et al. reference does not lack any element provided by the claims of the instant application, i.e., the instant claims require no more than is taught by the Watt et al. reference. Since the Barnett et al. reference teaches all the elements of the claims (both expressly and inherently), the patent anticipates the claimed invention

Conclusion

No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached 9:00 am - 5:30 pm EST (M-F).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached at (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gregory S. Emch/

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Patent Examiner
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10 April 2008

/Robert Landsman/
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